Restriction Requirement

In Paper 6, the Examiner issued a restriction requirement. Applicants elected Group III, claims 28 and 29, species SEQ ID NO: 2, species radioisotope, with traverse. Part of the reason for traverse was Applicants' contention that the description of Group 16, Claim 30 was incorrect, as Applicants felt it should be rewritten as drawn to a method of treating a disease state associated with inappropriate expression of PROST 03, comprising administering a ribozyme. The Examiner has disagreed, stating that "claim 30 clearly recites a method of treating a disease state associated with inappropriate expression of PROST 03, comprising administering a polypeptide of SEQ ID NO: 2, fragments or variants thereof". Claim 30 reads as follows:

"***A method of treating a disease-state in a human patient which disease-state is associated with inappropriate expression of PROST 03*** *and wherein the patient is in need of decreased levels of a polypeptide comprising a member selected from the group consisting of:*

(a) a polypeptide, or a biologically or immunologically active fragment thereof, comprising the amino acid sequence as set forth in Figure 2 (SEQ ID NO: 2); and

(b) a polypeptide which is at least 70% identical to the polypeptide of (a) and

wherein the method comprises administering to the patient a therapeutically effective amount of a ribozyme which specifically cleaves RNA encoding the polypeptide."

It is clear that the method comprises administering a ribozyme, not administering a polypeptide.

Sequence Rule Compliance

The Examiner has indicated that the legends for Figures 3 and 4 refer to sequences which lack sequence identification numbers. The Specification has been amended to indicate the appropriate SEQ ID numbers where necessary.

Rejection under 35 USC §112, second paragraph

The Examiner has rejected Claims 28 and 29 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 28 and 29 were dependent on non-elected Claim 24. Claims 28 and 29 have been amended to remove this dependency.

The amended Claims no longer use the language "biologically active fragment ...", which was contained in non-elected Claim 24, and which the Examiner found unclear.

Amended Claim 29 now contains the wording "a PROST 03 polypeptide having the amino acid sequence of SEQ ID NO: 2" to identify the claimed protein, removing the Examiner's concern over the use of "PROST 03" alone as the sole means of identifying the claimed protein.

Amended Claim 29 no longer uses the language "associated". Rather, Claim 29, as amended, is directed to the treatment of prostate-related disease. Applicants have shown that PROST 03 polypeptide expression is prostate specific (see Specification, pg 41 and Figure 5).

Rejection under 35 USC §112, first paragraph

The Examiner has rejected Claims 28 and 29 under 35 U.S.C. 112, first paragraph, as not containing a written description of the invention in sufficient detail.

Claims 28 and 29, as amended, no longer contain language relating to "biologically active fragment" or "an immunogenic fragment". Applicants believe the claims, as amended, render this rejection moot.

Rejection under 35 USC §112, first paragraph

The Examiner has rejected Claim 29 under 35 U.S.C. 112, first paragraph, because the Specification, while being enabling for a method for treating prostate carcinoma or metastatic prostate cancer, does not reasonably provide enablement for a method for treating a disease associated with the expression of SEQ ID NO: 2.

Applicants have amended Claim 29 to read "A method for treating prostate cancer", and believe the Examiner's rejection is, therefore, rendered moot.

Rejection under 35 USC §103

The Examiner has rejected Claims 28-29 under 35 U.S.C. 103(a) as being unpatentable over Xu et al. (US Patent No. 6,261,562), in view of Sinha (US Patent No. 6,379,669). Applicants respectfully traverse this rejection.

The Examiner has stated in the Office Action dated August 7, 2002, that the primary reference Xu et al. "teach a method for stimulating an immune response in a patient comprising administering a polypeptide of SEQ ID NO: 113. Under MPSRCH sequence similarity search, SEQ ID NO: 113 is 100% similar to the full length of the claimed SEQ ID NO: 2". Applicants acknowledge that SEQ ID NO: 113 of Xu et al. and Applicant's SEQ ID NO: 2 are identical.

However, as indicated by the Examiner, Xu et al. use this polypeptide or a portion of it to stimulate an internal immune response to prostate tumor cells within the patient. The Examiner further states, "Xu et al. **do not teach** a method for killing a cell expressing SEQ ID NO: 2 or a method for treating a disease-state in a patient, which disease state is associated with the expression of PROST 03, comprising administering an immunoconjugate of an antibody or fragment thereof, which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO: 2".

The secondary reference Sinha et al. teaches targeting and treatment of prostate cancer comprising administering immunoconjugates comprising an antibody specific for prostate specific antigen and a bioactive agent.

The Examiner suggests it would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to obtain an antibody specific for a prostate cancer specific antigen of SEQ ID NO: 113 for making an immunoconjugate and to target prostate cancer using such an immunoconjugate with a reasonable expectation of success.

Applicants respectfully submit that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. *In re Geiger*, 815 F.2d 686, 688; 2 U.S.P.Q. 2d 1276, 1278 (Fed. Cir. 1987). The mere fact that references can be combined does not render the resultant combination obvious. The Examiner, herself, indicates that

there is no suggestion in Xu et al. for killing prostate cells or treating prostate disease by targeting prostate cells with immunoconjugates directed to SEQ ID NO: 113.

Furthermore, Sinha, while suggesting that the immunoconjugate include a polyclonal or monoclonal antibody, prefers a polyclonal antibody (column 2, line 39), because "A polyclonal antibody has greater potential of recognizing many more epitopes of the substance associated with the solid tissue, e.g. PSA or (PACP) in the case of the prostate than a monoclonal antibody." (column 2, lines 43-52) and the Sinha patent specifically claims a polyclonal antibody (Claim 6). Amended Claims 28 and 29 of the instant application are specifically directed toward use of a monoclonal antibody. Thus, Applicants argue that even if one skilled in the art did combine the teachings of Xu et al. and Sinha, they would be directed toward generation of polyclonal antibodies, i.e. that the art actually teaches away from the instant invention as claimed.

Finally, Xu et al. do not disclose that SEQ ID NO: 113 (Applicants' SEQ ID NO: 2) is related to a family of membrane transport proteins, and that it is therefore a cell-surface protein. The knowledge that PROST 03 is membrane-bound, *which the Applicants have disclosed in the instant application* (Page 13, lines 9-12), is what makes PROST 03 an excellent target for a therapeutic immunoconjugate, ie. one used in a method to destroy a prostate cancer cell or treat prostate cancer. Antibodies to PSA, the well-known prostate cancer marker discussed by Sinha, while having proved useful for diagnosis, have not been reported as successful for therapy because the protein diffuses away from the tumor, so that any immunoconjugate directed to this marker does not target the tumor cell, per se, but binds to PSA in the serum. It is the Applicants' own findings regarding the membrane location of PROST 03 which might make one skilled in the art think that this polypeptide would prove useful as a therapeutic target for an immunoconjugate. The Examiner has not "taken into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made", but has included knowledge gleaned only from the Applicants' disclosure. See *In re McLaughlin*, 443 F.2d 1392: 170 USPQ 209 (CCPA 1971). The Examiner has relied on information which was present in the Applicants' disclosure and which became known to

one skilled in the art only at a later time. This is hindsight, and as such, is an impermissible basis for rejecting the invention.

In light of the amendments made to Claims 28 and 29 and the arguments provided above, Applicants respectfully submit that the rejection under 35 U.S.C. 103(a) has been overcome and respectfully request its withdrawal.

Conclusion:

Applicants respectfully submit that with the submission of the newly amended Claims 28 and 29 and the arguments presented above, the application is now in condition for allowance. Such action is solicited at an early date.

Respectfully submitted,

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VERSION WITH MARKING TO SHOW CHANGES

IN THE SPECIFICATION

On page 6:

FIGURE 3: Amino acid alignment of PROST 03 and DcSUT2, a sucrose/H+ symporter. The PROST 03 sequence **(SEQ ID NO: 2)** is on the bottom. The predicted transmembrane domains for each sequence are underlined.

FIGURE 4: Polynucleotide **(SEQ ID NO: 1)** and deduced amino acid **(SEQ ID NO: 2)** sequences of PROST 03.

IN THE CLAIMS:

28. (Amended) A method for selectively destroying a cell expressing **a PROST 03 polypeptide having the amino acid sequence of SEQ ID NO: 2, wherein the method comprises reacting** ~~the polypeptide of Figure 2 (SEQ ID NO: 2) comprising reacting~~ **an immunoconjugate comprising an isolated monoclonal antibody, or antibody fragment, which specifically binds to one or more epitopes present in the PROST 03 polypeptide conjugated to a therapeutic agent.** ~~immunoconjugate of Claim 24~~ with the cell so that the therapeutic agent of the immunoconjugate can destroy the cell.

29. (Amended) A method of treating **prostate cancer** ~~a disease state~~ in a human patient ~~which disease state is associated with expression of a PROST 03 polypeptide having the amino acid sequence of SEQ ID NO. 2~~, wherein the method comprises administering to the patient a therapeutically effective amount of **an immunoconjugate comprising an isolated monoclonal antibody, or antibody fragment, which specifically binds to one or more epitopes present in the PROST 03 polypeptide having the amino acid sequence of SEQ ID NO: 2, conjugated to a therapeutic agent.** ~~the immunoconjugate of Claim 24.~~